Utilizing Spectral-Domain Ocular Coherence Tomography to Determine Panretinal Photocoagulation’s Effect on Retinal Nerve Fiber Layer Thickness in Patients with Proliferative Diabetic Retinopathy

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Objective: To assess changes in RNFL after PRP using high resolution SD-OCT.

Introduction:
• Previous studies with variable results
• No prior studies using SD-OCT to examine peripapillary RNFL
• Why SD-OCT?
  - High resolution
  - Image Registration- inter-scan reproducibility
  - Less motion artifact
  - Faster scan acquisition
  - Why SD-OCT?
• No prior studies using SD-OCT to examine peripapillary RNFL
• Previous studies with variable results

Methods:
• IRB approved, prospective study
• Inclusion Criteria
  - First time PRP for High risk PDR
  - 360 degrees, >1000 spots, single treatment, supraquad or transequator lens
  - Any optic neuropathy or OHTN
  - Poor quality scans that could not be resegmented
  - Prisoners, pregnancy and those <18 yrs
• The Spectralis SD-OCT (Heidelberg Engineering Inc., Heidelberg, Germany) with image registration was used to measure pre-PRP RNFL thickness (global and regional) at follow-up visits

Exclusion criteria
• IRB approved, prospective study
• No prior studies using SD-OCT to examine peripapillary RNFL
• Why SD-OCT?
• Previous studies with variable results

Results:
• This study shows that after undergoing PRP, there is a significant increase from pre-PRP RNFL thickness in the 1-60 day, post-PRP period
• After the 60 day period, the RNFL thickness then plateaus and starts to trend downward.
• This change is most notable in the temporal peripapillary regions of the RNFL

Discussion:
• Long term changes in RNFL
• Our study shows that there is a statistically significant trend of RNFL thinning after PRP.
• It is unclear if these changes are secondary to PRP alone, diabetes, age, or some other factor.

Table 1
• Comparison between the 1-60d and 361-480d Post-PRP groups
• There is a significant trend toward thinning in the temporal regions

<table>
<thead>
<tr>
<th>1-60 days</th>
<th>Percent change in Pre-PRP RNFL thickness</th>
</tr>
</thead>
<tbody>
<tr>
<td>G</td>
<td>109.91%</td>
</tr>
<tr>
<td>TS</td>
<td>100.40%</td>
</tr>
<tr>
<td>T</td>
<td>100.69%</td>
</tr>
<tr>
<td>NI</td>
<td>111.13%</td>
</tr>
<tr>
<td>TI</td>
<td>113.50%</td>
</tr>
<tr>
<td>N</td>
<td>116.23%</td>
</tr>
<tr>
<td>S</td>
<td>107.69%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>361-480 days</th>
<th>Percent change in Pre-PRP RNFL thickness</th>
</tr>
</thead>
<tbody>
<tr>
<td>G</td>
<td>97.38%</td>
</tr>
<tr>
<td>TS</td>
<td>94.58%</td>
</tr>
<tr>
<td>T</td>
<td>113.46%</td>
</tr>
<tr>
<td>NI</td>
<td>91.35%</td>
</tr>
<tr>
<td>TI</td>
<td>91.99%</td>
</tr>
<tr>
<td>N</td>
<td>90.72%</td>
</tr>
</tbody>
</table>

Methods

• Hospital IRB Approved, prospective study

• **Inclusion Criteria**
  – Undergoing first-time PRP for treatment of high-risk proliferative diabetic retinopathy
  – Receiving at least 1000 spots, in a 360 degree fashion, and in a single treatment with a superquad and/or transequator lens

• **Exclusion Criteria**
  – Any prior history of optic neuropathy or ocular hypertension (IOPs >21 mmHg) on chart review
  – Poor quality scans that could not be re-segmented
  – Prisoners, pregnant patients, and those < 18 years of age were excluded

• The Spectralis SD-OCT (Heidelberg Engineering Inc., Heidelberg, Germany) with image registration was used to measure pre-PRP RNFL thickness (global and regional) at follow-up visits

• Because follow-up time varied based on clinical course, RNFL measurements were divided into four groups by time after PRP
  – 0-60 days, 61-120 days, 121-240 days, 241-360 days, and 361-480 days

• If significant segmentation errors were present, a single, blinded ophthalmologist re-drew the upper segment only

• Data was normalized by measuring percent change from pre-PRP RNFL values

• A two-sided, pairwise, t-test for the mean was used to determine significance of RNFL thickness changes (when compared to pre-PRP thickness) between each group
  – P-values <0.05 were considered significant

• Linear regression for each group was performed to assess long term changes and trends in the RNFL after PRP
Table 1:
• Summary of Data.
• Changes in RNFL thickness are compared to their pre-PRP values in the 5 groups.
• Global (G) thickness increased significantly in the 1-60d group.
• Inferonasal (NI), inferotemporal (TI), temporal (T), as well as superotemporal (TS) thickness also increased significantly in the 1-60d group.

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>Mean Days after PRP</th>
<th>G</th>
<th>NS</th>
<th>N</th>
<th>NI</th>
<th>TI</th>
<th>T</th>
<th>TS</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-60 days</td>
<td>12</td>
<td>42.5 ± 10.59 days</td>
<td>109.91%</td>
<td>105.40%</td>
<td>106.69%</td>
<td>111.13%</td>
<td>113.50%</td>
<td>116.23%</td>
<td>107.69%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Standard Deviation</td>
<td>9.52%</td>
<td>11.39%</td>
<td>17.71%</td>
<td>10.89%</td>
<td>10.77%</td>
<td>12.80%</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>p-value compared to pre-PRP</td>
<td>0.004</td>
<td>0.129</td>
<td>0.217</td>
<td>0.005</td>
<td>0.001</td>
<td>0.001</td>
</tr>
<tr>
<td>61-120 days</td>
<td>10</td>
<td>91.3 ± 15.32 days</td>
<td>107.83%</td>
<td>101.70%</td>
<td>103.72%</td>
<td>103.35%</td>
<td>99.47%</td>
<td>108.18%</td>
<td>101.44%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Standard Deviation</td>
<td>8.49%</td>
<td>8.31%</td>
<td>13.25%</td>
<td>8.31%</td>
<td>7.90%</td>
<td>18.78%</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>p-value compared to Pre-PRP</td>
<td>0.319</td>
<td>0.534</td>
<td>0.397</td>
<td>0.234</td>
<td>0.836</td>
<td>0.202</td>
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<tr>
<td>121-240 days</td>
<td>6</td>
<td>151.83 ± 26.25 days</td>
<td>103.06%</td>
<td>93.03%</td>
<td>107.46%</td>
<td>102.70%</td>
<td>107.66%</td>
<td>108.69%</td>
<td>102.93%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Standard Deviation</td>
<td>11.26%</td>
<td>20.68%</td>
<td>8.68%</td>
<td>13.13%</td>
<td>14.85%</td>
<td>23.23%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>p-value compared to Pre-PRP</td>
<td>0.535</td>
<td>0.447</td>
<td>0.089</td>
<td>0.636</td>
<td>0.262</td>
<td>0.402</td>
</tr>
<tr>
<td>241-360 days</td>
<td>9</td>
<td>285.22 ± 30.03 days</td>
<td>101.29%</td>
<td>97.95%</td>
<td>102.47%</td>
<td>99.88%</td>
<td>98.25%</td>
<td>112.89%</td>
<td>96.43%</td>
</tr>
<tr>
<td></td>
<td></td>
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<td>Standard Deviation</td>
<td>11.31%</td>
<td>9.44%</td>
<td>16.02%</td>
<td>11.86%</td>
<td>8.42%</td>
<td>24.98%</td>
</tr>
<tr>
<td></td>
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<td>p-value compared to Pre-PRP</td>
<td>0.741</td>
<td>0.534</td>
<td>0.656</td>
<td>0.976</td>
<td>0.551</td>
<td>0.160</td>
</tr>
<tr>
<td>361-480 days</td>
<td>6</td>
<td>398.17 ± 35.61 days</td>
<td>97.38%</td>
<td>94.58%</td>
<td>113.46%</td>
<td>101.62%</td>
<td>91.99%</td>
<td>91.40%</td>
<td>90.72%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Standard Deviation</td>
<td>21.31%</td>
<td>19.34%</td>
<td>36.30%</td>
<td>24.10%</td>
<td>17.27%</td>
<td>23.02%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>p-value compared to Pre-PRP</td>
<td>0.776</td>
<td>0.523</td>
<td>0.405</td>
<td>0.875</td>
<td>0.307</td>
<td>0.402</td>
</tr>
</tbody>
</table>
RNFL thickness increased in the 1-60 d in G, TS, T, TI, NI. (p<0.05).

1-60 d group vs 361-480 d group
TI: p=0.005
T: p=0.009
TS: p=0.022
G: p=0.099

Percent Change in RNFL thickness in the 1-60, 61-120, 121-240, 241-360, and 361-480 day post-PRP groups
Results: Is PRP associated with long-term RNFL thinning? Global trends.

- An 11% decrease in global thickness after 365 days

\[ y = -0.0003x + 1.0805 \]

\[ R^2 = 0.87832 \]

\[ p=0.006 \]
Discussion

- This study shows that after undergoing PRP, there is a significant increase from pre-PRP RNFL thickness in the 1-60 day, post-PRP period.
- After the 60 day period, the RNFL thickness then plateaus and starts to trend downward.
- This change is most notable in the temporal peri-papillary regions of the RNFL.
- Long-term changes in the RNFL
  - Multiple studies have shown that diabetics who undergo PRP have long-term thinning of the RNFL\textsuperscript{3,4,7}
- Our study also shows that there is a statistically significant trend of RNFL thinning after PRP.
  - Seen in the global thickness, as well as all temporal and the inferonasal regions
- It is unclear if these changes are secondary to PRP alone, diabetes, age, or some other factor.
- This is consistent with the findings of both Ritenour and Lee who found there to be an initial increase in RNFL thickness followed by a decline in thickness\textsuperscript{3,7}
- Muquit and Shimura found that macular thickness increases after PRP then returns to baseline after 6 months\textsuperscript{4,8}
  - This shows that untreated areas (the macula) can be affected by laser scars in the periphery
  - It is then possible, that the untreated peri-papillary RNFL could show thickening in a similar mechanism as macular thickening after PRP
- Our study shows that it is mainly temporal (i.e. macular) fibers that show significant change, this implies a common mechanism with macular thickening seen after PRP
- PRP also promotes contracture of fibrovascular tissue
  - Treatment may cause traction the peripapillary nerve fibers resulting higher observed RNFL thickness
  - This however, is unlikely to show a regional bias

Limitations

- No control group
- Retrospective nature of review
- Relatively small study that is not powered
- Re-segmentation of some scans

Conclusions

- PRP induces changes in the RNFL in the short and likely long-term
- These changes must be taken into account when using peri-papillary RNFL OCT measurements as a diagnostic tool
- Larger prospective trials are needed to confirm the results of this study
- Studies examining the specific etiology of this RNFL change are needed